

## **II. ARGUMENTS AND REMARKS**

### *1. Election/Restriction*

The Examiner requested cancellation of non-elected claims 1-77. *See page 2 of the office action.* Applicants cancel claims 1-77 without prejudice and reserve the right to present these claims in a duly filed divisional application.

### *2. Sequence Compliance Notice*

The Examiner requested that Applicants provide SEQ ID NO. for the oligonucleotide recited in claim 81. *See page 2 of the office action.* Applicants amend claim 81 with this response by providing the SEQ ID NO.

### *3. Claim Amendments*

Applicants add new claims 84 to 87 with this response and amend claim 78. Claim amendments as well as new claims do not introduce new matter and are fully supported by the specification as was filed.

### *4. Claim Rejections under 35 USC § 103 should be withdrawn*

Claims 78-82 continue to stand rejected under 35 U.S.C. § 103(a) as being unpatentable over *Hitoshi et al* (US 2002/0027167) in view of *Norton et al* (Nature Biotech., Vol. 14, pages 615-619,1996)) and *Page et al.* (Expl. Cell Res., Vol. 252, pages 41-49, 1999).

The Federal Circuit has stated that “rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.” *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d at 1396.

MPEP §2142 further provides that to reach a proper determination under 35 U.S.C. §103, an examiner must step backward in time and into the shoes worn by the hypothetical “person of ordinary skill in the art” when the invention was unknown and just before it was made. *Id.* In view of all factual information, the examiner must then make a determination whether the claimed invention “as a whole” would have been obvious at that time to that person. *Id.*

The pending claims as amended with this response, recite a composition comprising an oligonucleotide with at least 50% sequence identity to (TTAGGG)<sub>n</sub> and with nucleotide linkages in this oligonucleotide being hydrolyzable by a 3' to 5' nuclease. Claim 79 further provides that this 3' to 5' nuclease can be Mre11. The Examiner relied on *Page* and *Norton* for disclosure of specific sequences in connection with the obviousness analysis.

Applicants turn Examiner’s attention to the *Page* reference. As clearly stated in the abstract, the goal of the *Page* study was to block the telomerase activity and this goal was achieved by providing NON-HYDROLYZABLE oligonucleotides. *See Materials and methods.* Accordingly, Tables 1 and 2 disclose oligonucleotides which are non-hydrolyzable. These non-hydrolyzable oligonucleotides cannot be used a substrate for a 3' to 5' nuclease, while pending claims are limited only to those oligonucleotides that are hydrolyzable by a 3' to 5' nuclease.

*Page* does not mention MRE11 (or any other 3' to 5' nuclease) and instead *Page* is focused on telomerase. Thus, there is no disclosure in *Page* as to what a suitable substrate for a 3' to 5' nuclease is in general and for MRE11 in particular.

*Norton* is deficient in the same way as *Page*. This reference is also concerned with the studies in which the telomerase activity is inhibited by NON-HYDROLYZABLE peptide nucleic acids (PNAs). The *Norton* PNAs cannot be utilized as a substrate for nuclease and further, *Norton* does not disclose a suitable substrate for a 3' to 5' nuclease in general and MRE11 in particular.

The Examiner has previously agreed that *Hitoshi* does not teach or suggest the synthetic substrate sequences instantly claimed.

The Examiner agrees that *Page* and *Norton* do not disclose any sequences with internucleotide linkages that can be hydrolyzed by a 3' to 5' nuclease in general and MRE11 in particular. *Hitoshi* is silent about the substrate as now recited by the pending claims. The only reasoning for combining *Page* and *Norton* with *Hitoshi* that the Examiner has provided was applicant's disclosure, which is impermissible hindsight and must be avoided. Applicants respectfully submit that a person of skill would not have had a reason for considering the oligonucleotides disclosed in *Page* and *Norton*, which are disclosed only for blocking a telomerase, and then using these oligonucleotides as a substrate for an absolutely different enzyme, 3' to 5' nuclease, such as MRE11, and then further modifying these oligonucleotides.

Because the *Hitoshi/Page/Norton* combination does not disclose or suggest oligonucleotides that can be used as a substrate for a 3' to 5' nuclease, such as MRE11, the combination fails to teach or suggest at least some elements as recited by the pending claims and therefore, the *prima facie* case of obviousness has not been established. Further, since there was no other reason to combine the references, but Applicants'

disclosure, the *Page/Norton/Hitoshi* combination is based on impermissible hindsight and therefore, the *prima facie* case of obviousness has not been established for this reason as well.

Because no *prima facie* case of obviousness has been established, the Examiner may properly withdraw the rejection of the pending claims under 35 U.S.C. §103(a), and Applicants respectfully request this withdrawal.

**III. CONCLUSION**

Applicants respectfully submit that the instant application is in good and proper order for allowance and early notification to this effect is respectfully solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at (312) 595-1408.

Respectfully submitted,  
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